ORIGINAL ARTICLE

MRI Features of Intracranial Fungal Granuloma Taking Histopathology as the Gold Standard

MUHAMMAD ASIF, SHAHID MEHMOOD, TANWEER AHMED
Department of Radiology and Neurosurgery, Lahore General Hospital, Lahore

ABSTRACT

Objective: *To explain the MRI features of intracranial fungal granuloma in patients with histopathology confirmed fungal infection.*

Material and Methods: *This descriptive case series study was conducted at the department of Radiology and Neurosurgery Lahore General Hospital, Lahore from June 2012 to June 2014, two years duration. 40 patients with histopathology confirmed intracranial fungal granuloma were included in this study. The mean ± SD was 33.76 ± 5.43 years. Out of total 40 patients 24 (60%) male and 16 (40%) female patients.*

Study Design: *Descriptive Case Series.*

Duration: *Two Years from June 2012 – June 2014.*

Setting: *Department of Radiology and Neurosurgery, Lahore General Hospital, Lahore.*

Introduction: *The diagnosis of intracranial fungal granulomas almost always remained a challenge both for neurosurgeons and radiologists because of their alter behavior and radiology. The diagnosis of these infections has increased in recent years because of increased awareness among clinicians about this pathology, better diagnostic tools and increase in the number of immunocompromised hosts (from any cause). Although mortality and morbidity from central nervous system (CNS) mycosis has improved over years; mortality often reaches 80 – 100% if the disease is not diagnosed properly and management initiated at the earliest. This study will help us to describe different radiological features (MRI) of this disease so that early detection and better management can be initiated on time.*

Results: *This study included 40 patients having histopathology confirmed diagnosis of intracranial fungal granuloma. The mean ± SD was 33.76 ± 5.43 years. Out of total 40 patients 24 (60%) male and 16 (40%) female patients. Thus the male to female ratio was 1.5: 1. Most of the patients were in their second and third decade of life. Out of total 40 cases, there were 36 (90%) patients had Aspergillus type and only 4 (10%) patients had Mucormycosis type of fungal infection.*

Conclusion: *These infections are hypo – iso intense on T2W MRI images with no or minimal enhancement in immunocompromised individuals. In immunocompetent individuals these infections form granuloma and usually show post gadolinium MRI enhancement.*

Abbreviations: *MRI (Magnetic Resonance Imaging), CNS (Central Nervous System).*

Key words: *Aspergillosis, Mucormycosis, immunocompromised, immunocompetent, hyperintense, hypointense, magnetic resonance imaging.*

INTRODUCTION

Intracranial fungal infections are widely diagnosed these days because of increased awareness among clinicians about this pathology and better diagnostic tools. These infections are most common among immunocompromised, cancer and chemotherapy pati-

ents, HIV infected patients, diabetics and intravenous drug abusers (Anwar et al, 2009; Selvam et al, 2010; Ramesha et al, 2010).

Imaging is extremely important in the management of immunocompromised host with suspected intracranial fungal infection mainly because early diagnosis and vigorous treatment are the key factors in improved outcome. Furthermore, if the condition of the patient permits imaging also provides a tool for tissue sampling and longitudinal treatment. The use of MRI also narrows the differential diagnosis of such kind of infections. Intracranial fungal granuloma present with non specific clinical and radiological features and are often mistaken for a tumor or abscess. In the brain these infections most commonly affect the corticomedullary junctions owing to increased vascularity, spread from the nearby structures such as the paranasal sinuses and ears. Hematogenous spread to the brain from a focus in the lungs is very rare. Environmental pollution, hot and dry weather with high concentration of agricultural dust plays an important role in the development of the disease (Azarpira et al, 2008; Anwar et al, 2009; Valecha et al, 2014).

This study will help us to formulate radiological guidelines for the disease so that better management can be planned.

MATERIALS AND METHODS

This descriptive case series study was conducted at the department of Radiology and Neurosurgery Lahore General Hospital, Lahore from June 2012 to June 2014, two years duration. 40 patients with histopathology confirmed intracranial fungal granuloma were included in this study. The mean ± SD was 33.76 ± 5.43 years. Out of total 40 patients 24 (60%) male and 16 (40%) female patients. Thus the male to female ratio was 1.5: 1. Most of the patients were in their second and third decade of life. Out of total 40 cases, there were 36 (90%) patients had Aspergillus type and only 4 (10%) patients had Mucormycosis type of fungal infection. MRI brain plain and contrast was done in all patients at admission. After histopathology confirmation of intracranial fungal granuloma, antifungal treatment started and only these patients were included in the study. The MRI features of these patients were compared and where necessary MRI (both plain and contrast) was repeated. These patients were followed both radiologically and symptomatically for six months. The MRI findings were evaluated

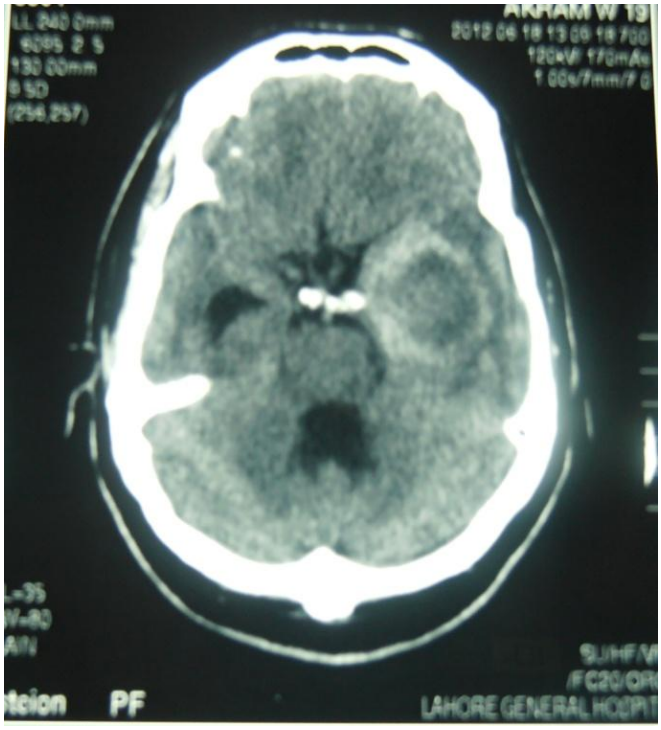

Fig. 1: Computed tomography scan of a patient with aspergillosis showing hyperdense lesion in the left temporal lobe.

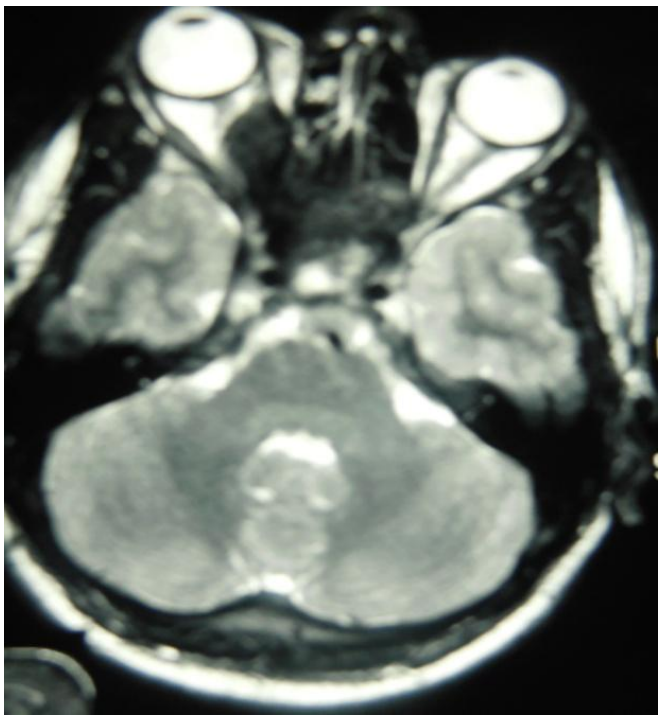

Fig. 2: Magnetic resonance T_2W image of a patient with aspergillosis showing iso to hypointense lesion involving the right cavernous and sphenoid sinuses.

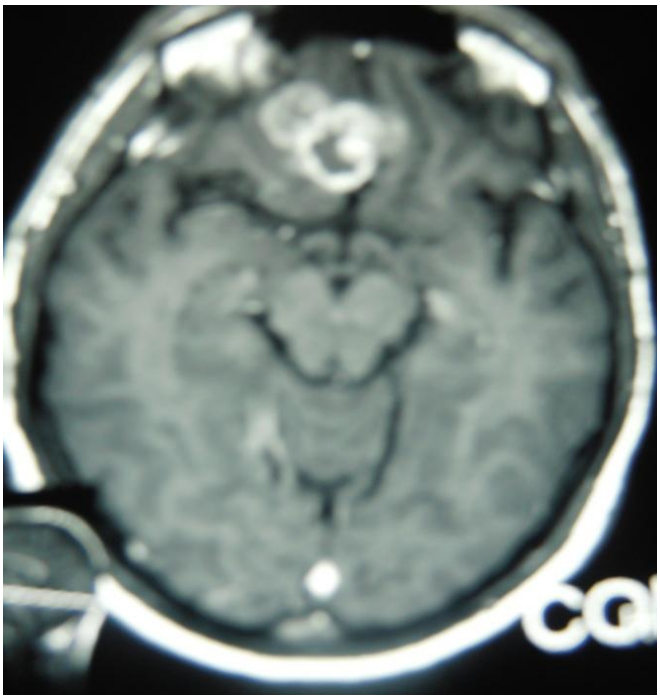

Fig. 3: Magnetic resonance imaging with gadolinium of a patient with aspergillosis showing heterogeneous ring enhancing lesion in the right cavernous and sphenoid sinuses.

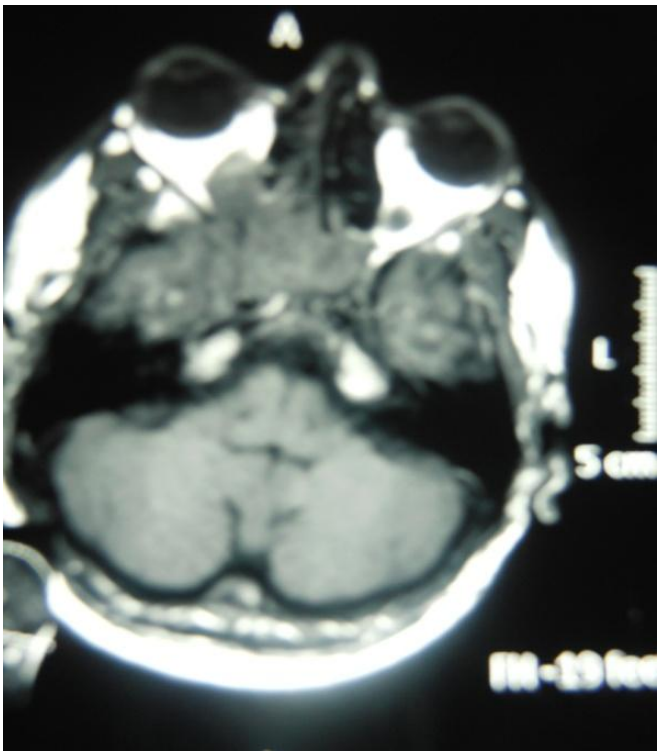

Fig. 4: Magnetic resonance T_1W image of a 35 year old male with aspergillosis showing signals change in left temporal lobe.

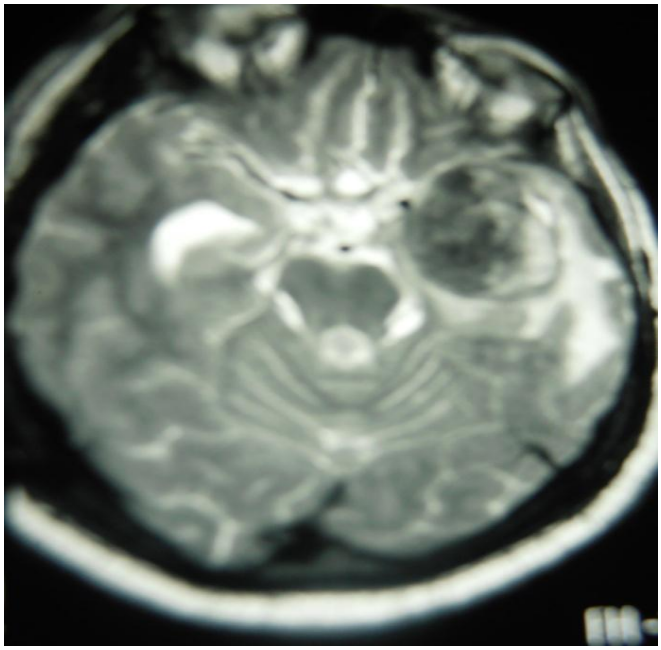

Fig. 5: Magnetic resonance T_2W image of a 35 year old male with aspergillosis showing heterogeneous mostly hypointense signals in left temporal lobe.

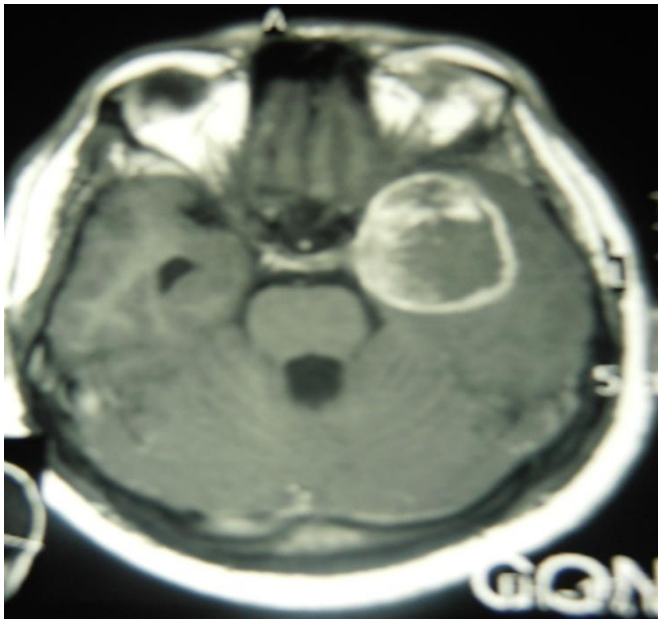

Fig. 6: Magnetic resonance imaging with gadolinium of a patient with aspergillosis showing heterogeneous ring enhancing lesion in left temporal lobe.

for site of lesion, signal characteristics, hemorrhage and progression on serial images when repeated.

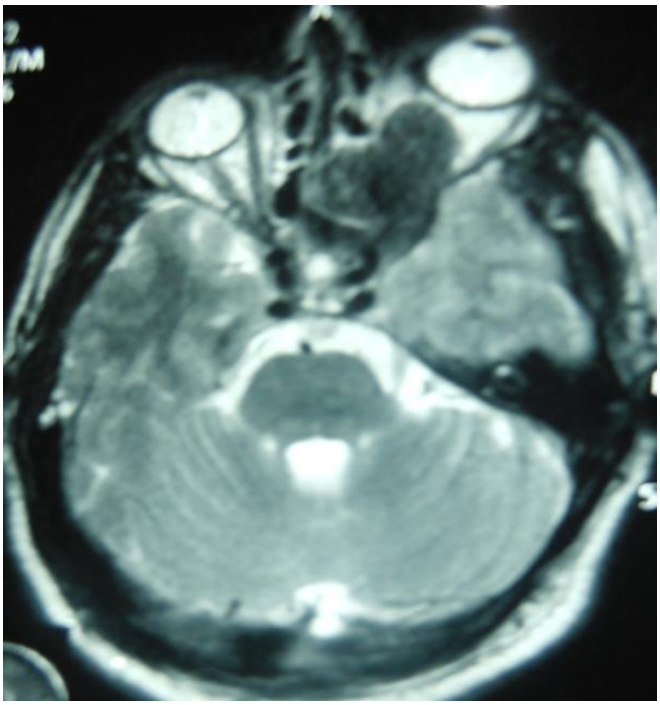

Fig. 7: Magnetic resonance T_2W image of a patient with aspergillosis showing hypointense lesion in the left Ethmoidal and orbital area.

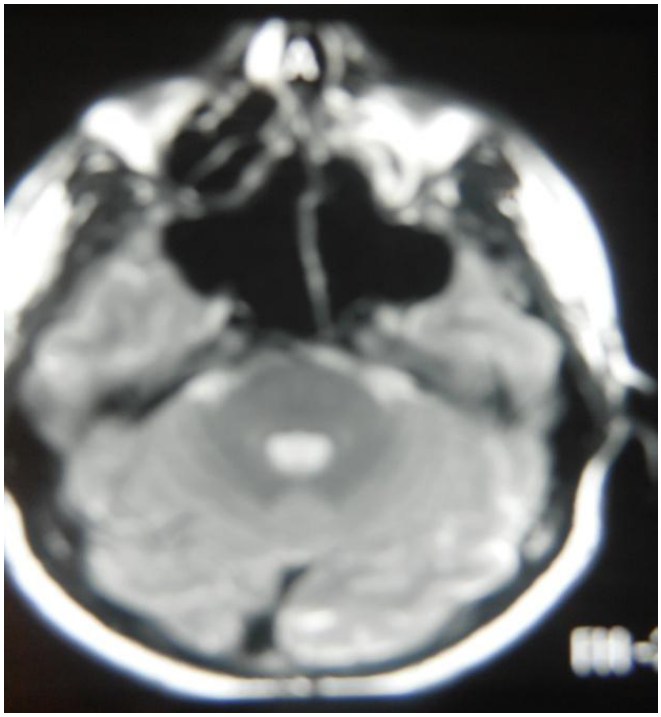

Fig. 9: Magnetic resonance T2W image of a patient with aspergillosis showing hypointense lesion at the base of skull.

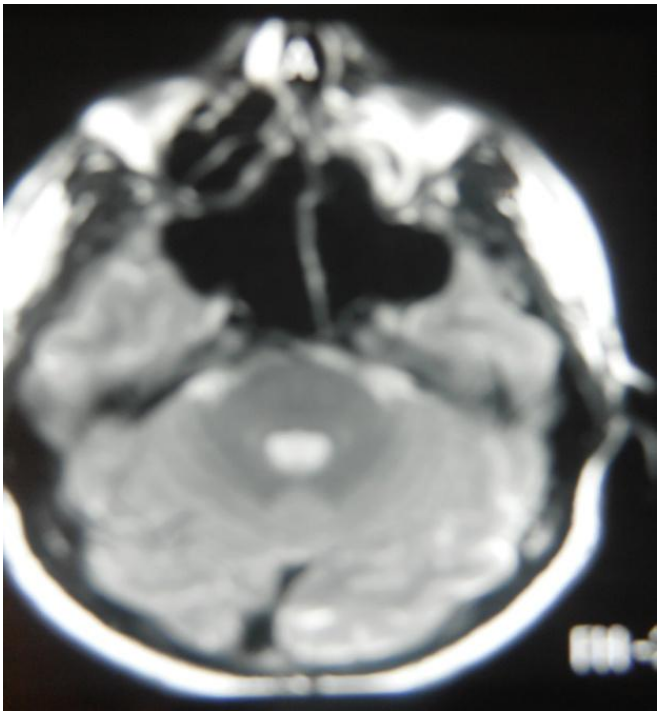

Fig. 8: Magnetic resonance T2W image of a patient with aspergillosis showing hypointense lesion at the base of skull.

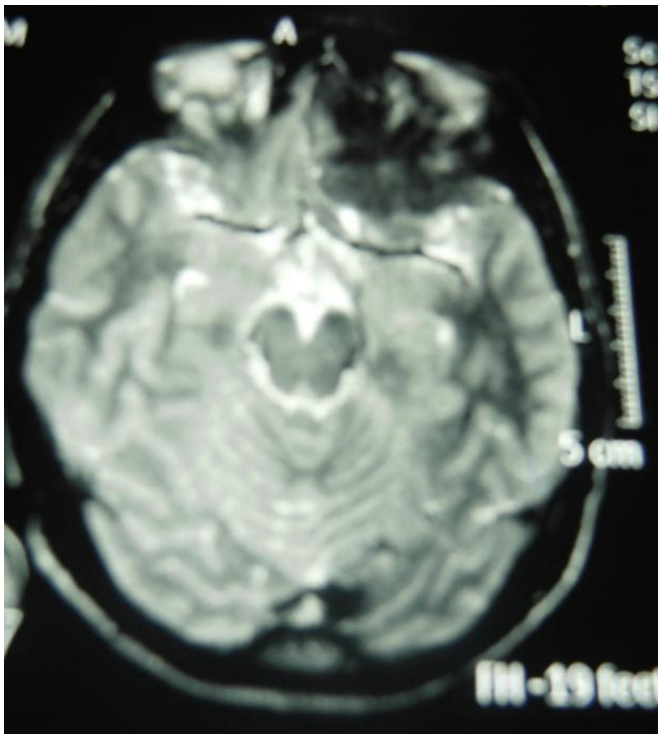

Fig. 10: Magnetic resonance T2W image of a patient with aspergillosis showing hypointense lesion in the left orbital area.

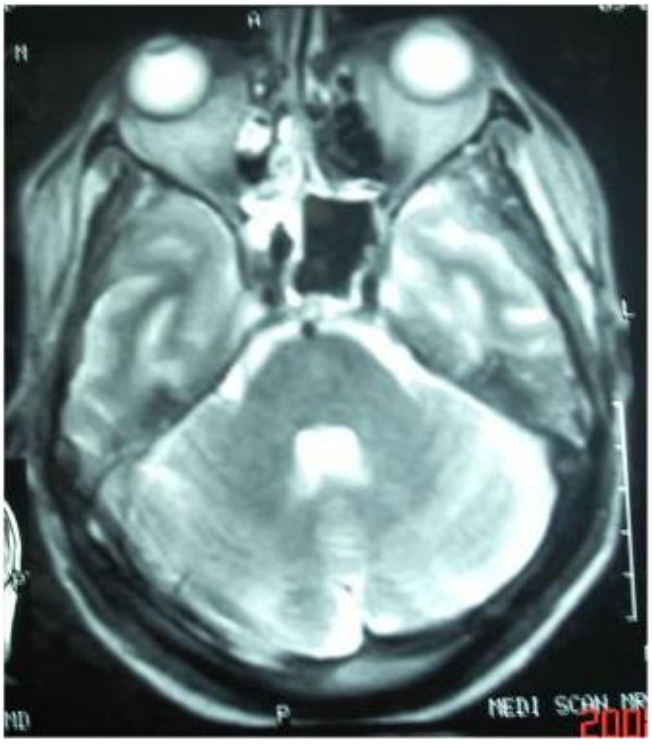

Fig. 11: MRI T_2w image of patient with mucormycosis showing hypointense lesion involving the ethmoid and sphenoid sinuses.

RESULTS

Outcome of intracranial fungal granuloma depends on the immune status of the patient. In immunocompromised hosts mortality reaches more than 90% and up to 100% in some cases. However, in immunocompetent hosts mortality ranges between 60% and 80%. Furthermore, the prognosis is better whenever the granuloma is extradural compared with intradural fungal granuloma. The prognosis is worst when there is involvement of the brain parenchyma and vascular invasion. In the brain these infections commonly affect the corticomedullary junction owing to increased vascularity (M. Turgut et al, 2008; Muhammad et al, 2010; Valecha et al, 2014).

All the 40 patients had supratentorial intracranial fungal granuloma. 22 patients had sinuses (sphenoid, ethmoid and cavernous sinus) infection, 8 patients had orbital, 4 temporal, 4 parietal and 2 patients had frontal fungal infection. Post gadolinium MRI enhancement appreciated in few patients. After aggressive antifungal therapy there was no progression of the disease process. Hemorrhage and aneurysm was not found in any of the patients.

Table 1: *Age Distribution of Patients (n = 40).*

Age Years	No. of Patients	Percentage
20 – 30	20	50.0
31 – 40	12	30.0
41 – 50	6	15.0
51 – 60	2	5.0

Mean ± SD = 33.76 ± 5.43

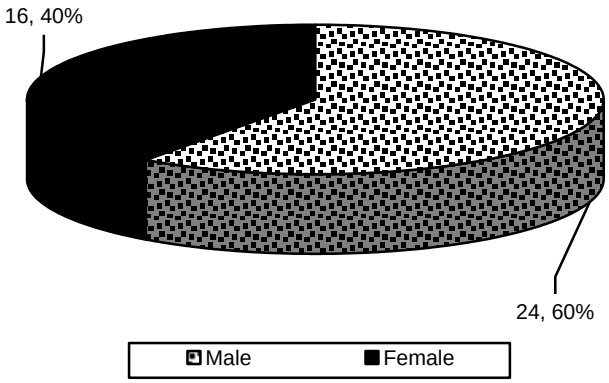

Fig. 12: *Sex Distribution of Patients.*
Sex Distribution of Patients (n = 40)
Male to female ratio = 1.5:1

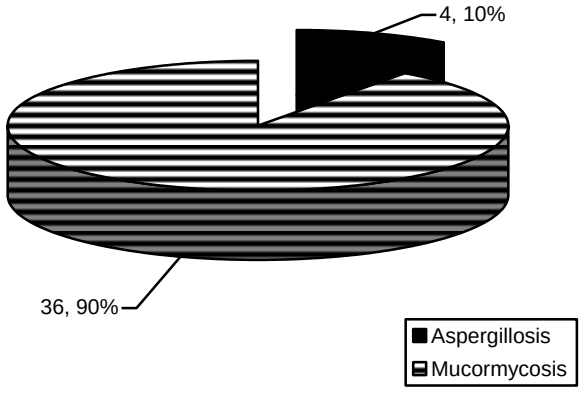

Fig. 13: *Common Types of Fungus.*

DISCUSSION

Intracranial fungal granulomas most commonly affect the areas of brain that are adjacent to the sinuses, the frontal and the parasellar areas. Primary intracranial fungal granuloma is rare and it often spreads hematogenously / directly from infected sinuses, the mastoid

and lungs, so a detailed examination of these primary sites should be carried out in patients having intracranial fungal granuloma as well as the immune status of the individual. Radiologically these lesions resemble granulomas, meningitis, mycotic aneurysms, infarcts and tumors. In aspergillosis there is invasion of the blood vessels leading to infarction/ hemorrhage or aneurysm formation seen radiologically. Granuloma formation occurs in immunocompetent hosts. These lesions appear hypointense on T_1 – weighted MR images, hypo to iso – intense on T_2 – weighted MR images with vague / absent or either bright homogenous or ring enhancement of contrast material. The hypointensity of these lesions is mainly due to coagulative necrosis and dense fungal hyphal population. These findings are proven histologically but are not specific. Furthermore, these lesions also contain iron, manganese and magnesium leading to altered MR signal intensities / hypointensities. In immunocompromised hosts these lesions have usually a hypointense ring having a greater tendency for hemorrhage. However, in immunocompetent hosts there is usually an irregular dense enhancement ring (Muhammad et al, 2010; Valecha et al, 2014).

The differential diagnosis of multiple brain lesions in an immunocompromised host include; lymphoma, metastasis, septic disease, multiple infarcts and fungal infections. Lack of enhancement excludes lymphoma, metastasis and other primary brain tumors, with strong suspicion of fungal infections especially if the host is immunocompromised and antifungal therapy should be initiated at the earliest (Amy et al, 2006; Muhammad et al, 2010; Valecha et al, 2014).

CONCLUSION

Intracranial fungal granuloma is relatively uncommon, affecting mostly the immunocompromised and rarely the immunocompetent individuals. Despite better diagnostic tools preoperative radiological diagnosis of intracranial fungal granuloma is difficult. For diagnosis a high index of suspicion, proper clinical, radiological and hematological evaluation, timely histopathology and aggressive antifungal treatment is necessary for effective eradication of the infection (Muhammad et al, 2010; Valecha et al, 2014). These lesions appear hypointense on T_1 – weighted MR images, hypo to iso – intense on T_2 – weighted MR images with vague / absent or either bright homogenous or ring enhancement of contrast material. In immunocompromised hosts these lesions have usually a hypointense ring having a greater tendency for hemorrhage. However, in immunocompetent hosts there is usually an irregular dense enhancement ring. If the individual is immunocompromised and there is no MRI enhancement after gadolinium then there is a strong suspicion of intracranial fungal granuloma (Muhammad et al, 2010; Valecha et al, 2014).

Address for correspondence:
Dr. Muhammad Asif
PGR Department of Radiology
Lahore General Hospital, Lahore
Contact: 0333-8755411
E-mail: drasifmughal_83@yahoo.com

REFERENCES

1. Amy, D., Richard, E., Joacim, F., Edward, S. Cerebral Aspergillosis: Radiologic and Pathologic Findings. J RadioGraphics, 2006; 26: 1239-1242.
2. Anwar, M., Fauzia, S., Khalid, M., Zafar, I., Naveed, A., Tariq, S. Intracranial fungal granuloma various treatment modalities depending upon the anatomical structures involved. Pak J Neurol Surg, 2009; 13 (1): 1-11.
3. Azarpira, N., Esfandiari, M., Bagheri, HM., Rakei, S., Salari, S. Cerebral aspergillosis presenting as a mass lesion. Brazilian J Infect Dise, 2008; 12 (4): 349-51.
4. Arvind D, Ravish VP, Sammana S, Vani S, Sastry K, Anil N. Intracranial fungal granuloma: analysis of 40 patients and review of the literature. Surgical Neurology, 2005; 63: 254–60.
5. Baig, MM., Niazi, AK., Niazi, FAK., Najeeb, T. Rhino-Orbito-Cerebral Mucormycosis: Clinical presentation and outcome. Ann Pak Inst. Med Sci. 2009; 5: 8-11.
6. Casey, A.T., Wilkins, P., Uttley, D. Aspergillosis infection in neurosurgical practice. Br J Neurosurg, 1994; 8: 31-9.
7. Chakrabarti, A. Epidemiology of central nervous system mycoses. Neurol India, 2007; 55: 191-97.
8. Challa, S., Uppin, GS., Purohit, KA. Isolated cerebral Aspergillus granuloma with no obvious source of infection. Neurology India, 2007; 55 (3): PP. 289-91.
9. Denning, D.W., Stevens, D.A. Antifungal and surgical treatment of invasive aspergillosis: Review of 2121 published cases. Rev Infect Dis, 1990; 12: 1147-201.
10. Dhiwakar, M., Thakar, A., Bahadur, S. Improving outcomes in rhinocerebral mucormycosis – early diagnostic pointers and prognostic factors. J Laryngol Otol, 2003; 117: 861-65.
11. Dubey, A., Patwardhan, R.V., Sampath, S., Santosh, V., Kolluri, S., Nanda, A. Intracranial fungal granuloma: Analysis of 40 patients and review of the literature. Surg Neurol, 2005; 63: 254-60.
12. Dupont, B. Fungal infections of the central nervous sys-

tem. In: Anaissie EJ, McGinnis MR, Pfaller MA, eds. Clinical Mycology. 1st ed. Churchill Livingstone: New York, 2003: P. 539-53.
13. Eileen, PS., Lindsey, R., Baden, Joel, TK. Fungal brain infections. Current Opinion in Neurol, 2008; 21: 347–52.
14. Gupta, S. A man with sudden loss of vision and ptosis: Clin Optometry, 2010; 2: 25–27.
15. Jain, K.K., Mittal, S.K., Kumar, S., Gupta, R.K. Imaging features of central nervous system fungal infections. Neurol India, 2007; 55: 241–50.
16. Kara, I.O., Tasova, Y., Uguz, A., Sahin, B. Mucormycosis – associated fungal infections in patients with haematologic malignancies. Int J Clin Pract. 2007.
17. Kleinschmidt-DeMasters, B.K. Central nervous system aspergillosis: a 20 – year retrospective series. Hum Pathol. 2002; 33: 116–24.
18. Kontoyiannis, D.P., Marr, K.A., Park, B.J. Prospective surveillance for invasive fungal infections in hematopoietic stem cell transplant recipients, 2001 – 2006: overview of the Transplant-Associated Infection Surveillance Network (TRANSNET) Database. Clin Infect Dis, 2010; 50: 1091–100.
19. Middelhof, C.A., Loudon, W.G., Muhonen, M.D., Xavier, C., Greene, C.S. Jr. Improved survival in central nervous system aspergillosis: A series of immunocompromized children with leukemia undergoing stereotactic resection of aspergillomas. Report of four cases. J Neurosurg, 2005; 103: 374-8.
20. Muhammad, S.S., Syed, A. E., Rushna, A., Saleha, A. Craniocerebral Aspergillosis: A review of advances in diagnosis and management. JPMA, 2010.
21. Muhammad, S.S., Arshad, A.S., Syed, A.I., Ahmed, A.S., Rashid, J., Saleha, A. Craniocerebral aspergillosis in immunocompetent hosts: Surgical perspective. Neurol. India, 2007; 55 (3): 274-81.
22. Mullins, M.E. Emergent neuroimaging of intracranial infection/inflammation. Radiol Clin. North Am., 2011; 49 (1): 47-62.
23. Nithyanandam, S., Jacob, M.S., Battu, R.R., Thomas, R.K., Correa, M.A., D'Souza, O. Rhino-Orbito-Cerebral Mucormycosis: A retrospective analysis of clinical features and treatment outcomes. Indian J Ophthalmol, 2003; 51: 231-6.
24. Ostrow, T.D., Hudgins, P.A. Magnetic resonance imaging of intracranial fungal Carrazana, E.J., Rossitch, E. Jr, Morris, J. Isolated central nervous system aspergillosis in the acquired immunodeficiency syndrome. Clin Neurol Neurosurg, 1991; 93: 227–30.
25. Ostrow, T.D., Hudgins, P.A. Magnetic resonance imaging of intracranial fungal infections. Top Magn Reson Imaging, 1994; 6: 22–31.
26. Petrikkos, G., Skiada, A., Sambatakou, H., Toskas, A., Vaiopoulos, G., Giannopoulou, M., Katsilambros, N. Mucormycosis: ten-year experience at a tertiary-care center in Greece. Eur J Clin Microbiol Infect Dis. 2003; 22: 753-56.
27. Ramesha, K.N., Kate, M.P., Kesavadas, C., Radhakrishnan, V.V., Nair, S., Thomas, S.V. Fungal infections of the central nervous system in HIV-negative patients: Experience from a tertiary referral center of South India. Ann Indian Acad Neurol. 2010; 13: 112-6.
28. Saini, J., Gupta, A.K., Jolapara, M.B., Chatterjee, S., Pendharkar, H.S., Kesavadas, C., Radhakrishnan, V.V. Imaging findings in intracranial aspergillus infection in immunocompetent patients. World Neurosurg., 2010; 74 (6): 661-70.
29. Selvam M, Pande A, Chakravarthy VM, Ramamurti R. Invasive rhino-cerebral fungal granuloma: Neurol India, 2010; 58 (2): 270-76.
30. Mehmet, T., Yelda, O., Serkan, O., Orhan, A., Mustafa, B., Ertugrul, Cengiz, T., Berna, G., Serhan, S. Invasive fungal granuloma of the brain caused by Aspergillus fumigatus: a case report and review of the literature. Surg. Neurol. 2008; 69: 169-174.
31. Valecha J, Gupta V, Garg N. Cerebral aspergilloma mimicking tumoral mass: A diagnostic dilemma. West Afr J Radiol. 2014; 21: 87-90.

AUTHORS DATA

Name	Post	Institution	E-mail
Dr. Muhammad Asif	PGR	Department of Radiology and Neurosurgery, Lahore General Hospital, Lahore	drasifmughal_83@yahoo.com
Dr. Shahid Mehmood			
Dr. Tanweer Ahmed			